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| 10/019,954 | 05/24/2002 | Eric Samain | 065691-0267 | 6242 |
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| FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007 | | | EXAMINER PROUTY, REBECCA E | |
| | | | ART UNIT 1652 | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/019,954 | Applicant(s) SAMAIN ET AL. | |
| | Examiner Rebecca E. Prouty | Art Unit 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-7,9-12,15-17,21-24 and 27-48 is/are pending in the application.
- 4a) Of the above claim(s) 15-17,21-24,29,31-38 and 40-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5-7, 9-12, 27, 28, 30, 39, 47, and 48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Claims 2-4, 8, 13, 14, 18-20, 25, and 26 have been canceled. Claims 1, 5-7, 9-12, 15-17, 21-24, and 27-48 and are still at issue and are present for examination.

Claims 15-17, 21-24, 29, 31-38, and 40-46 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/13/05.

Applicants' arguments filed on 10/18/07, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 1 and 48 are objected to because of the following informalities: "Lac" should be inserted prior to "Z-Y". Appropriate correction is required.

Claim 2 is objected to because of the following informality: "sulfation" is misspelled.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 47 is confusing in the recitation of "exposing said cell to lactose permease under conditions sufficient to induce internalization of said exogenous precursor" as it is unclear under what conditions lactose permease will internalize sialic acid. Applicants state that they have amended Claim 47 such that sialic acid is no longer recited as an exogenous precursor but this is not in fact true. Claim 47 is further confusing in the recitation an E. coli cell having a *LacZ*⁻, *LacY*⁺, *NanA*, or *NanT*⁺ genotype as this fails to make clear whether *NanA* is present or absent. Furthermore it is unclear how some of these genotypes are relevant to the instant claims. Did applicants intend "or" to be "and"?

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the

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applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bettler et al. in view of Kozumi et al. The rejection is explained in the previous Office Action.

Applicants argue that one of skill in the art would have no motivation to combine Bettler and Kozumi, much less any expectation of success as it was known in the art that rapid uptake of sugars by lactose permease disrupts membrane function, possibly by causing collapse of the membrane potential and results in growth inhibition and eventually cell death (i.e., lactose killing). Given this knowledge in the art, a skilled artisan would have no reason to combine the teachings of Bettler and Kozumi, much less have an expectation of success. However, this is not persuasive because lactose killing as reported in the references previously cited by applicants in the response of 5/30/06 is present in *E coli* cells that have been growing on a limited supply of lactose when they are then provided with excess lactose but not in cells growing on other carbon sources when supplied with lactose (see Dykhuizen et al.) and the claims have now been amended to in fact recite first growing the cells to high levels on a carbon based substrate which is preferably

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glucose or glycerol (first phase of culturing) and only then adding the lactose in the second phase of culturing. Thus this matches exactly the conditions under which the references teach lactose killing does not occur. Furthermore, as reported in Ahmed et al. the amount of growth inhibition produced by lactose can be diminished by reducing the rate of import of lactose into the cell (see Ahmed et al. and Dykhuizen et al.) and the presence of glucose/glycerol in the culture during the second phase of cell growth would do just that as they are well known to repress the lactose promoter. Furthermore, a skilled artisan would be aware that even a low growth rate of the cells during the second phase could still be sufficient to produce large amounts of the desired product. In fact artisans would clearly be aware that many products of interest produced in bacteria are produced only at the end stage of a fermentation when the cells are only growing slowly or have stopped growing and skilled artisans are clearly provided with the tools (i.e., inducible promoters) to control the rate of production of the lactose permease such that the rate of influx of lactose could adjusted so as to limit lactose influx mediated growth inhibition. As such a skilled artisan would not have lacked motivation of expectation of success in view of the disclosures cited by applicants.

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Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bettler et al. in view of Kozumi et al. as applied to claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 above, and further in view of Johnson and Gotschlich (WO 96/10086).

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/447,287. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 5-7, 9-12, 27, 28, 47, and 48 of the instant application and claims 1-13 of copending Application No. 11/447,287 are all directed to methods of producing an oligosaccharide comprising lactose using a genetically modified microorganism transformed with at least one glycosyltransferase gene by culturing the cell in the presence of lactose as an exogenous precursor. The claims differ in that the claims of the copending application are limited to the synthesis of oligosaccharides comprising a sialyllactose while the claims of the instant application broadly read on any oligosaccharide comprising lactose and the claims of the instant application recite that the microorganism is particularly a *LacZ*⁺ *E. coli* and that the culturing comprises a first phase of growth on a carbon based substrate in the absence of lactose which substrate is preferably glucose or glycerol and a second phase of growth limited by the carbon base substrate which is

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added continuously wherein lactose is added during the second phase while the claims of the copending application are not limited in the scope of the microorganism or the method of culturing. However, the specification in copending Application No. 11/447,287 makes it clear that use of a *LacZ⁻Y⁺ E. coli* as the microorganism (paragraph 48) and culturing as recited in the instant claims (Example 1) are preferred embodiments of the recited methods. Claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 cannot be considered patentably distinct over claims 1-13 of copending Application No. 11/447,287 when there is a specifically preferred embodiment of the copending application that would anticipate claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 herein. Alternatively, claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 herein cannot be considered patentably distinct over claims 1-13 of copending Application No. 11/447,287 when there is a specifically disclosed embodiment in the copending application that supports claims 1-13 of the copending application and falls within the scope of claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 herein because it would have been obvious to one having ordinary skill in the art to modify the method of claims 1-13 of the copending application by selecting a specifically preferred microorganism and culturing method. One having ordinary skill in the art would have been motivated to do

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this because that embodiment is disclosed as being a preferred embodiment within claims 1-13.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56 of copending Application No. 11/509,818. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 5-7, 9-12, 27, 28, 47, and 48 of the instant application and claims 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56 of copending Application No. 11/509,818 are all directed to methods of producing an oligosaccharide comprising lactose using a genetically modified microorganism transformed with at least one glycosyltransferase gene by culturing the cell in the presence of lactose as an exogenous precursor. The claims differ in that the claims of the copending application are limited to the synthesis of oligosaccharides comprising a galabiose motif while the claims of the instant application broadly read on any oligosaccharide comprising lactose and the claims of the instant application

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recite that the microorganism is particularly a *LacZ⁻Y⁺ E. coli* and that the culturing comprises a first phase of growth on a carbon based substrate in the absence of lactose which substrate is preferably glucose or glycerol and a second phase of growth limited by the carbon base substrate which is added continuously wherein lactose is added during the second phase while the claims of the copending application are not limited in the scope of the microorganism or the method of culturing. However, the specification in copending Application No. 11/509,818 makes it clear that use of a *E. coli* as the microorganism (paragraph 65) and culturing as recited in the instant claims (Example 1) are preferred embodiments of the recited methods. Claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 cannot be considered patentably distinct over 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56 of copending Application No. 11/509,818 when there is a specifically preferred embodiment of the copending application that would anticipate claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 herein. Alternatively, claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 herein cannot be considered patentably distinct over 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56 of copending Application No. 11/509,818 when there is a specifically disclosed embodiment in the copending application that supports claims 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56 of

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the copending application and falls within the scope of claims 1, 5-7, 9-12, 27, 28, 39, 47, and 48 herein because it would have been obvious to one having ordinary skill in the art to modify the method of claims 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56 of the copending application by selecting a specifically preferred microorganism and culturing method. One having ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims 1-3, 7, 8, 11-14, 18, 20, 21, 24, 30, 34-51, and 56.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on

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access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
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